change in CD59 mRNA levels was insignificant. While the abundance of transcripts encoding MAC components and CD59 drop to insignificant values thereafter, expression of C3 remained significantly greater than control at days 5 and 9 (3.5 and 3.1-fold, p = 8.05E-22 and 2.15E-05, respectively).
Conclusions: Most complement activators, MAC components and inhibitors were significantly upregulated in the synovium after ACL transection. Although further characterization of the complement activation in human knee joints after ACL injury is needed, the porcine model may be a relevant preclinical model for the testing of therapeutic candidates for blocking the complement response of the joint after injury.

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HYDROSTATIC PRESSURE INDUCES INCREASED PRODUCTION OF TGF-β VIA ERK ACTIVATION IN SYNOVIAL FIBROBLASTS FROM RZAT TEMPOROMANDIBULAR JOINT

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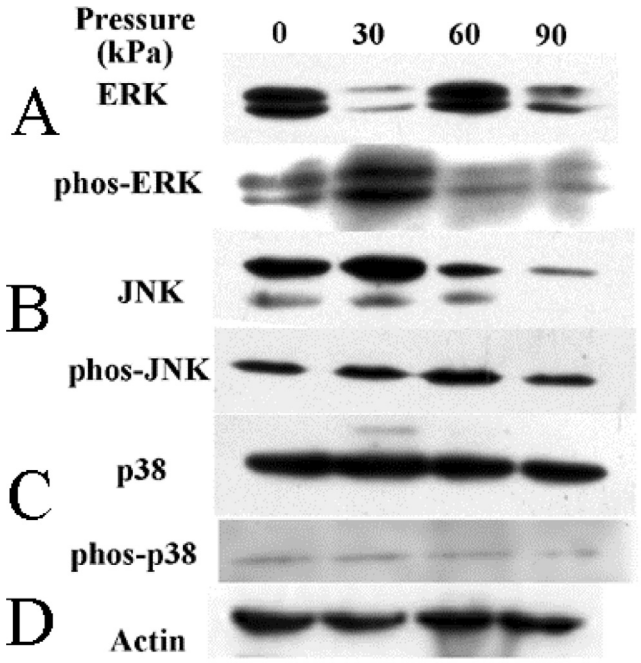
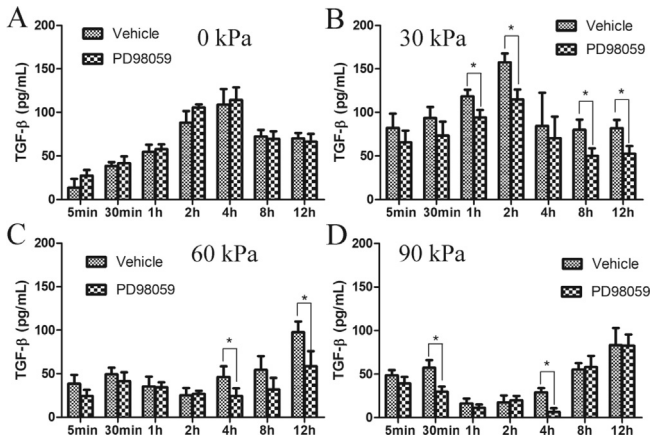
Purpose: TGF-β plays important roles in proliferation, differentiation, and transition of fibroblasts. The objective of present study was to investigate whether the release of TGF-β was correlated to the magnitude of hydrostatic pressure (HP) in synovial fibroblasts (SFs) from rat temporomandibular joint, and explore its potential relationship with activation of MAP kinase pathway.
Methods: SFs isolated from double condyles of rat temporomandibular joint were treated with hydrostatic pressures (HP) of 30, 60, and 90 kPa HP for 12 hours. The production of transforming growth factor-beta (TGF-β) in SFs suffered with different HP was determined by ELISA from 5 minutes to 12 hours in absence and presence of ERK1/2 inhibitor (PD98059). Furthermore, the activation of ERK1, JNK and p38 MAPKs in response to the treatment of hydrostatic pressure were examined by Western blot.
Results: Compared with untreated control, the level of TGF-β dramatically increased in synovial with hydrostatic pressure of 30 kPa from 5 minutes to 4 hours, while co-treatment of PD98059 can attenuate the increase. The TGF-β production was slightly increased in synovial with higher pressure (60 and 90 kPa), while PD98059 can also reduce the increase. Hydrostatic pressure can significantly up-regulated the phosphorylation of ERK1/2 in SFs, whilst significant activations of JNK and p38 were not observed.
Conclusions: TGF-β is generally thought to play an important role in bone development, remodeling and osteogenesis. According to our findings, SFs treated with PD98059 caused a decrease in TGF-β production stimulated by HP, indicating that the ERK1/2 pathway is essential for the enhancement of TGF-β production induced by HP.





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SYNOVIAL EXPRESSION OF CCL19 AND ITS RECEPTOR CCR7 IN PATIENTS WITH MENISCAL PATHOLOGY: VARIABILITY AND RELATIONSHIP WITH KNEE SYMPTOMS

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Purpose: Although patients with meniscal tears are at increased risk for progressive OA, the relationship between meniscal pathology and knee symptoms is not clear. In a previous pilot study, we demonstrated that synovitis is associated with worse knee symptoms and dysfunction in patients undergoing partial meniscectomy, mRNA expression levels of the chemokine CCL19 and its receptor CCR7 were associated with presence of synovitis, and also strongly correlated with knee symptoms. But many patients indicated for meniscal arthroscopy already have early-stage OA, unlike the patients included in the pilot who had normal knee radiographs. Therefore, we tested whether similar relationships between CCL19, CCR7 and symptoms could be found in more typical patients presenting for meniscal arthroscopy. In addition, we sought to determine whether CCL19 and CCR7 protein expression in synovial fluid (SF) and synovial membrane (SM), respectively, varies with symptomatic knee disease.
Methods: SF and SM specimens were collected during surgery from patients undergoing meniscal arthroscopy. SM biopsies for mRNA analysis were available from 19 patients, and SF from 32 patients. SM mRNA for CCL19 and CCR7 was measured using real-time PCR, and SF CCL19 measured by ELISA (R&D systems). The KOOS (Knee Injury and Osteoarthritis Outcome Score) was administered preoperatively, and measures knee symptoms and dysfunction in 5 separate domains: pain, other symptoms, activities of daily living (ADL), sport and recreation function, and knee-related quality of life (QOL). Pearson's correlations were used to determine relationships between mRNA or SF levels and KOOS scores. Multivariable linear regression models were run to test if associations were independent of age, gender, BMI, cartilage degeneration (measured using Outerbridge Classification) and radiographic OA (Kellgren-Lawrence) scores. Synovial CCR7 expression was characterized using immunohistochemical (IHC) staining, and compared to staining in SM from advanced OA patients and asymptomatic post-mortem donors.
Results: The majority of meniscal patients had grade 2-4 Outerbridge scores and median K/L scores of 2, indicative of pre-existing OA. CCL19 and CCR7 transcripts were detected in all patients. CCL19 relative expression (RE) was associated with KOOS ADL (r = -0.620, p = 0.005), Pain (r = -0.547, p = 0.015), and QOL scores (r = -0.479, 0.038), and multivariate models showed CCL19 RE was independently associated only with KOOS ADL scores (β = -4.201, 95% CI [-8.071, -0.331], p = 0.036). CCL19 protein was detectable in SF from 25/32 patients (78%), and mean concentration+/-SD was 374.28+/-367.58 pg/m. In unadjusted correlations, SF CCL19 concentration was also associated with worse KOOS-ADL subscores (Pearson r = -0.362, p = 0.049), but this was not independent of other factors in adjusted regression analyses. IHC

staining identified CCR7 expression in the synovial lining layer, endothelium, and perivascular inflammatory infiltrates. Staining patterns were similar in meniscal and advanced OA patients, and in both patient groups was more pronounced than in asymptomatic organ donors.
Conclusion: This current study extends our previous findings by demonstrating a relationship between synovial CCL19 mRNA expression and knee-related difficulty with activities of daily living in typical patients presenting for arthroscopic meniscal surgeries. Although SF CCL19 protein was detectable in the majority of these patients, protein levels were not independently associated with knee symptoms. However, the receptor CCR7 was increased in patients compared with asymptomatic donors. Its expression by multiple cell types in synovium suggests that CCL19/CCR7 activity may be involved in development of synovitis in these patients.

Therapy - Non-Pharmacologic

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HIGHER BASELINE QUADRICEPS STRENGTH IS PROTECTIVE AGAINST INCIDENT RADIOGRAPHIC KNEE OA IN OVERWEIGHT AND OBESE WOMEN

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Purpose: Higher Quadriceps strength is thought to be protective against incident knee OA. Given the increased muscular requirements to control joint loads in overweight and obese individuals, this effect might even be greater in this population. The purpose of the present study is to evaluate the relationship between baseline Quadriceps strength and incident knee OA in subjects at high risk; middle-aged overweight and obese women, free of signs of knee OA.
Methods: We used data from the PROOF study. For this study, all women between 50 and 60 years registered at 50 general practitioners in the area of Rotterdam, the Netherlands, were contacted. All willing women with a BMI $\geq$ 27 kg/m2 and without knee complaints were invited for baseline measurements. All 407 included women filled in a questionnaire regarding knee complaints (including KOOS, VAS pain, number of days with knee pain) and physical activity (SQUASH questionnaire) and underwent physical examination and radiography of both knees. Isometric Quadriceps strength was measured in supine position, with the knee slightly flexed. A handheld dynometer was held at the distal part of the tibia and provided with resistance while the subject was asked to maximally extend their knee. Force in Newton was divided by body weight in kg. Based on the maximal score of three trials, subjects were divided in three equal groups; low, average and high strength. The primary outcome was incident knee OA, defined as incidence of K&L $\geq$ 2, the ACR-criteria, or joint space narrowing (JSN) $\geq$ 1.0 mm after 30 months. All knees with K&L $<$ 2 at baseline, with complete follow-up data were selected for the analyses. Using Generalising Estimating Equations, the association between Quadriceps strength and incident knee OA (primary outcome and all sub definitions separately) was determined for the average and high strength group, relative to the low strength group, adjusted for other baseline differences between groups and the randomized groups of the original trial.
Results: In total, 639 knees from 335 women were included in the analyses. Baseline characteristics are given in the Table 1. After 30 months, 17% of all knees showed incident knee OA. A trend towards a preventive effects in the highest strength group was found for the primary outcome (Table 2). This was probably driven by the incidence of radiographic knee OA, since the highest strength group had a significantly lower odds ratio for the incidence of K&L $\geq$ 2 compared to the lowest strength group.
Conclusions: Higher baseline isometric Quadriceps strength reduced the risk for incident radiographic knee OA after 30 months in overweight and obese women. Since the mean difference between the lowest and highest strength groups was only 1.5 N per kg body weight, strength training of knee extensors seems to be a simple and safe intervention to prevent radiographic knee OA in overweight and obese subjects.

Table 2
Incidence of knee OA and associated adjusted ORs for incident knee OA

Outcome	Low strength	Average strength	High strength
Knee OA	21% (reference)	19% 0.9 (0.5 - 1.7)	12% 0.6 (0.3 - 1.1)
Medial JSN	6% (reference)	5% 1.1 (0.4 - 2.7)	4% 0.9 (0.3 - 2.6)
Lateral JSN	5% (reference)	9% 1.8 (0.7 - 4.7)	5% 1.1 (0.4 - 3.1)
ACR criteria	7% (reference)	5% 1.0 (0.4 - 3.0)	4% 0.9 (0.3 - 2.6)
K&L $\geq$ 2	10% (reference)	4% 0.5 (0.2 - 1.4)	2% 0.3 (0.1 - 0.9)

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PREOPERATIVE EFFECTS OF PROGRESSIVE EXPLOSIVE_TYPE RESISTANCE TRAINING IN PATIENTS WITH OSTEOARTHRITIS SCHEDULED FOR TOTAL HIP ARTHROPLASTY – A PROSPECTIVE RANDOMIZED CLINICAL TRIAL

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Purpose: Hip Osteoarthritis (OA) is associated with pain, functional deterioration and loss of muscle function. Progressive explosive-type resistance training (RT) is effective in improving muscle strength and functional performance in healthy elderly. In hip OA patients the effects prior to THA remain unknown. The Purpose was to investigate the effect of progressive explosive-type RT in hip OA patients scheduled for THA on i) self-reported outcomes and ii) muscle function, physical function and body composition.
Methods: RCT. Eighty patients (age 70.4 $\pm$ 7.6 years, BMI 27.8$\pm$4.6, 70% females(n = 52)) diagnosed with hip OA and scheduled for primary THA were randomized into two groups: 1) The intervention group (IG) received supervised progressive explosive-type RT twice a week for 10 weeks; 4 exercises of 3 series each ($\sim$80% of 1 repetition max). 2) The control group (CG) received 'care as usual'. Outcomes: Primary; Hip Osteoarthritis Outcome Score (HOOS), secondary; leg extension power, functional tests, body composition (DXA). Adjusted between group changes from baseline to follow-up (2-5 days prior to surgery) were analyzed as intention-to-treat using multilevel regression.
Results: For HOOS ADL the IG scored 9.7 points 95%CI [4.3;15.2] higher compared to CG at follow-up (p = 0.001). For the remaining

Table 1
Baseline characteristics (* $p < 0.05$)

	All	Low strength	Average strength	High strength
N (knees)	639	199	209	231
Strength (N/kg)	2.92 $\pm$ 0.6	2.3 $\pm$ 0.4*	3.1 $\pm$ 0.2*	3.8 $\pm$ 0.4*
Age (yr)	55.7 $\pm$ 3.2	55.8 $\pm$ 3.0	55.9 $\pm$ 3.2	55.3 $\pm$ 3.3
BMI (kg/m2)	32.0 $\pm$ 3.9	34.2 $\pm$ 4.5*	32.0 $\pm$ 3.6*	30.0 $\pm$ 2.3*
Physical activity (SQUASH)	6860 $\pm$ 3634	6274 $\pm$ 3249*	6657 $\pm$ 3774*	7547 $\pm$ 3722*
History of knee injury	12%	13%	14%	9%
Postmenopausal status	68%	66%	72%	72%
Heberden nodes	26%	29%	27%	24%
K&L = 1	45%	54%*	38%*	43%*
Mild knee symptoms	28%	36%*	26%*	22%*
Varus alignment	39%	40%	36%	40%